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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,665	07/01/2003	Jacob Nielsen	10165-022-999	5726

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EXAMINER	
DUTT, ADITI	

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1649	

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12/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/612,665	NIELSEN ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *1-53 and 59-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-58 and 71-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendix A*.

DETAILED ACTION

Status of Claims

1. The amendment filed on 30 June 2008 has been entered into the record and has been fully considered. Claims 54-58 are amended. New claims 71-73 have been added.

Species Withdrawal

2. On further consideration of the current amendment of claims 54 and 57 reciting amino acid substitution at one or more residues of SEQ ID NOs: 1-4 of SEQ ID NO: 10, the finality of the restriction requirement for the species election of a single EPO point mutation is withdrawn. All mutein species are rejoined and will be examined to the extent that they read upon a substitution of an amino acid residue at one or more positions of SEQ ID NOs: 1, 2, 3 or 4 as recited in claims 54 and 57.

Traversal of withdrawal of claims 69 and 70

3. Applicants traverse the withdrawal of claims 69 and 70 from examination in the last Office Action dated 12/31/07. Applicants argue that the claims are within the scope of their antecedent claim 57 that recites a method for protecting

or preventing a tissue injury using an EPO mutein. Applicants cite paragraphs from the specification to prove that the administration of the mutein before a surgical procedure is a specific embodiment of the method of claim 57. Because claims 69 and 70 would not require additional searches, Applicants request the consideration of claims 69 and 70 in the current Office Action.

4. Applicant's arguments are fully considered but not found to be persuasive, because as per restriction requirement dated 6/20/06 pages 17-19), Applicants elected "retinal ischemia" as the species of injury (see Applicant's response dated 12/20/06, page 5, election (h)), without traverse. Since each of the listed injury type will involve different cell types, determine characteristically different pathology, requiring different treatment strategies, from one another, each will represent a patentably distinct invention and would require a separate search of the art that would be burdensome to the examiner. Besides the limitations 'surgical procedure', or a 'cardiopulmonary bypass surgery', of claims 69 and 70 form a different species commensurate with the original "heart-lung bypass" (see Office Action dated 6/20/06, page 18, species number (xxvii)) species, that is distinct from the elected "retinal ischemia". Lastly, Applicant's allegation that the administration of the EPO mutein before a surgical procedure is a specific embodiment of the method of claim 57 is inappropriate, because the limitation reciting "surgical procedure" is not present in claim 57. Narrow limitation contained in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. See *In re Philips*

Industries, Inc. v. State Stove & Mfg. Co., 522 F.2d 1137, 186 USPQ 458 (CA6 1975), 237 PTJA A-12. While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See Ex parte Oetiker, 23 USPQ2d 1641 (BPAI, 1992). Applicant is reminded that the claims define the subject matter of his invention and that the specification cannot be relied upon to read limitations into the claims. Claims 69 and 70 are therefore, withdrawn as directed to non-elected species.

5. Claims 54-58, and 71-73, drawn to a method for protecting, maintaining or enhancing the viability of a responsive cell by administering a tissue protective cytokine in vivo or ex vivo, are under consideration in the instant application.

6. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

7. Applicant's arguments filed on 30 June 2008, have been fully considered. New grounds of objection and rejection are as follows.

Response to Amendment

Withdrawn objections and/or rejections

8. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (30 June 2008).

9. Upon consideration of current claim amendments reciting substitution in specific regions of the EPO sequence of SEQ ID NO: 10, and Applicant's persuasive arguments, rejection of claims 54-58, under 35 USC § 102(b) as anticipated by Campana et al has been withdrawn.

Claim rejections maintained

Double Patenting

10. Applicants have requested that the rejections be held in abeyance until the indication of allowable subject matter is presented. The rejections will be maintained of record until the submission of terminal disclaimers.

35 U.S.C. § 112, first paragraph – Scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. The rejections of claims 54-58, are applied to the amended claims and new claims 71-73, for reasons of record in the Office Action dated 31 December 2007.

12. Claims 54-58 and 71-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of protecting, maintaining or enhancing the viability of an erythropoietin-responsive cell, tissue or organ isolated from a mammalian body; or a method of protecting tissue injury, or restoring or rejuvenating tissue function in a mammal wherein the tissue is responsive to EPO; comprising exposing said cell, tissue or organ, in vivo or in vitro to a pharmaceutical composition comprising a mutein tissue protective cytokine comprising SEQ ID NO: 10, wherein the mutein consists of S100E, R150E, R103E K45D or K45D/S100E, and has a reduced level of in vivo erythropoietic activity, does not reasonably provide enablement for the method comprising exposing said cell, tissue or organ in vivo or in vitro, to a pharmaceutical composition comprising any mutein recombinant tissue protective cytokine comprising SEQ ID NO: 10, with a substitution of any amino acid residue at one or more positions of SEQ ID NOs: 1, 2, 3 or 4, as broadly claimed.

The specification is also not enabled for the prevention of a tissue injury or restoring or rejuvenating tissue in a mammal comprising administering any mutein recombinant tissue protective cytokine as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the inventions commensurate in scope with these claims.

13. The claims recite ex vivo method of protecting, maintaining or enhancing the viability of a responsive cell (neuronal or ganglion), or an organ comprising exposing said cell, tissue or organ to a pharmaceutical composition comprising a mutein tissue protective cytokine comprising the amino acid sequence of SEQ ID NO: 10, with a substitution of an amino acid residue at one or more position of SEQ ID NOs: 1, 2, 3 or 4, has reduced in vivo erythropoietic activity, and has tissue protective activity (claims 54-56, 71). Claims 57-58 and 72-73 are drawn to an *in vivo* method of protecting against tissue injury, prevention of tissue injury, or restoration or rejuvenation of tissue or tissue function, in a mammal using the above muteins, wherein the mammal has or is at risk of a large number of diseases and injuries, e.g. retinal ischemia.

14. Applicants believe that the amended claims 54-58 and the new claims 71-73 are enabled to the entire scope because the claims recite a method of tissue protection using a defined class of EPO muteins with amino acid substitutions at a limited number of amino acid residues. Additionally the amended claims provide a test to determine whether the mutein possesses the required activity of

tissue protection and reduced in vivo erythropoietic activity. Applicants assert that the amended claims enable the skilled person to practice the invention without undue experimentation.

15. Applicants submit a Declaration of Michael L. Brines, M.D., Ph.D., dated 29 June 2008, which is considered and acknowledged. The Declaration is effective in clarifying the tissue protective activity of EPO in many tissue injuries because of the presence of the tissue protective receptor complex in most tissues.

EPO Muteins

16. Applicants assert that the limited number of EPO muteins have specific structural and functional characteristics required for tissue protection while having reduced ability to stimulate erythropoiesis. Specifically, the muteins have amino acid substitutions in regions affecting the binding to the Classical EPO receptor, thereby reducing erythropoietic activity, without affecting the binding to the Tissue Protective Receptor Complex (TPRC), thus maintaining the tissue protective function. Applicants provide evidence by citing working examples for the use of EPO muteins in the instant specification, wherein the muteins have in vitro and/or in vivo tissue protective activity, for example using S100E, R103E or R150E muteins in reducing neuronal cell death in vitro (see e.g. Examples 3, 14, 15, 17; Brines Declaration) or administering muteins S100E in reducing functional deficits in motor neurological function in a traumatic spinal cord injury

animal model or using S100E or R103E for tissue protection in an animal model of glaucoma in vivo (Examples 12, 18).

17. Applicant's arguments are fully considered, however, are found to be persuasive in part. While the current claim amendments have limited the number of claimed muteins by specifying substitutions in specific regions of the mature polypeptide sequence of EPO of SEQ ID NO: 10, the claims still broadly read on a large number of sequences with one or more substitutions in SEQ ID NOs 1-4. As such the broadest reasonable interpretation of the amended claims would be an ex vivo or in vivo method encompassing the use of a mutein tissue protective cytokine comprising the peptide sequence of SEQ ID NO: 10, with a substitution of one or more amino acid **with any amino acid** in SEQ ID NOs: 1, 2, 3 or 4, wherein the mutein has a reduced in vivo erythropoietic activity and, wherein the mutein has tissue protective activity (emphasis added). Examiner agrees to Applicant's comments asserting the evidence of specific muteins in working examples demonstrating the claimed activity in vitro or in vivo or both. Examiner also agrees that muteins S100E, R103E, R150E, K45D, K45D/S100E have shown tissue protection, especially S100E and R103E for in vivo reduction of retinal injury and spinal cord injury. The Brines Declaration and Applicant's Remarks cite examples of tissue protection using both chemically modified EPO and EPO muteins by one or more amino acid substitution. The specification teaches the making of muteins by various modifications including substitution, addition, and deletion of amino acids in SEQ ID NOs: 1-4 and various other

positions (pages 4-9; 32-35; 47-49), that can be tested and used for tissue protection. However, the specification has not provided sufficient guidance about specific muteins with substitution at specific amino acid residues and demonstrating the claimed properties. This information is essential to the skilled artisan because in all likelihood all sequences identical to SEQ ID NO: 10 and having one or more substitution in the above 4 regions will not result in the desired activity. For example, Gantier et al. (US PGPB 20080194477A1, dated 8/14/2008) teach a modified EPO peptide (para 0357) of sequence (SEQ ID NO: 942), that is identical to the instant SEQ ID NO: 10, except for a point mutation in K45Q (see attached Appendix A for SCORE sequence alignment; also see insert below). The reference teaches that the modified cytokine and EPO peptides have increased bioavailability and increased resistance to proteolysis (para 0258-0259), however, have the same therapeutic properties of the unmodified cytokine involving erythropoietic activity, such as in red blood cell expansion, anemia, renal failure, cancer etc. (para 0443; Table, page 103). The reference also provides various modifications by substitution of amino acids in the EPO sequence, many of which are within the regions of the instantly claimed SEQ ID NOs: 1-4, wherein all muteins protect against proteolysis without the reduction in erythropoietic activity (Figure 12L). However, with the exception of muteins S100E, R103E, R150E, K45D, K45D/S100E, the instant specification has not provided guidance on the broad genus of muteins as claimed. Without this information the specification's general discussion of making and using of muteins

constitute an invitation to experiment by trial and error. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). Undue experimentation would be required by the skilled artisan to determine such. Based on the broad genus of muteins as recited in the amended claims, a skilled artisan will require undue experimentation to test the enormous number of putative muteins, involving the substitution of 20 amino acids in 28 different positions of SEQ ID NO: 10. Undue experimentation will be required of the skilled person to test the muteins having tissue protective activity along with reduced erythropoietic activity.

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US-11-704-141-942

 Query Match             99.5%;  Score 847;  DB 3;  Length 166;
 Best Local Similarity   99.4%;  Pred. No. 1.5e-88;
 Matches  165;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 APPRLICDSRVLERYLLEAKEAENITTGCAEHCSLNENITVPDTKVNFYAWKRMEVGQQA 60
              |||||||||||||||||||||||||||||||||||||||||||||:|||||||||||||||
Db          1 APPRLICDSRVLERYLLEAKEAENITTGCAEHCSLNENITVPDTQVNFYAWKRMEVGQQA 60

Qy         61 VEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLRSLTTLLRALGAQKEAIS 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        121 PPDAASAAPLRTITADTFRKLFRVYSNFLRGKLKLYTGEACRTGDR 166
              |||||||||||||||||||||||||||||||||||||||||||||
Db        121 PPDAASAAPLRTITADTFRKLFRVYSNFLRGKLKLYTGEACRTGDR 166
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Protection or Rejuvenation of tissues

18. Applicants assert that because the Tissue Protective Receptor Complex (TPRC) is present on a large variety of tissues, EPO muteins with reduced erythropoietic activity are tissue protective in a broad range of diseases and injuries involving a wide range of tissues. Applicants, therefore, allege that the claimed EPO muteins can have tissue protective activity "regardless of the source of the injury, other symptoms of the disease of condition, and the cell type affected" (see Brines Declaration). Applicants also assert that while the skilled artisan would understand that a certain amount of experimentation and optimization is required to determine the right dosage and the efficacy of a particular EPO mutein, the safety and effectiveness of a product should be left to the Food and Drug administration, and the patent requirement should not be confused with this issue. Finally, Applicants clarify the interpretation of the terms "restore" and "rejuvenate" stating that the terms in the claims "does not require new cell growth but only that the function of the tissue or organ is restored". Applicants provide Example 10 from the instant specification, wherein the treated mice exhibit restoration of cognitive function. Because of the above reasons, Applicants assert that the skilled artisan can readily determine the making and using of the claimed invention without undue experimentation, thus request the withdrawal of the enablement rejection.

19. Applicant's arguments are fully considered, but found to be persuasive in part. Examiner accepts the argument that because TPRC is present in a wide

variety of tissues, EPO muteins with the claimed activity will exhibit protection in a wide range of responsive cells and tissues, in different injury states. However, as stated above the claims still broadly read on a huge number of muteins, entailing undue experimentation in recognizing the right mutein having the claimed characteristics of tissue protection and reduced erythropoietic property. Besides, as TPRC is present in a wide range of tissues, the response will depend on the receptor concentration, binding affinity, and binding specificity to the muteins. As stated in the previous Office Action, the art recognizes in vivo and in vitro protective effect of erythropoietin (EPO) on ischemic injury models and certain immune mediated inflammatory responses using EPO and EPO recombinant variants like K45D, R103E, R150E, and S100E. However, the art and the instant specification fail to provide guidance on the making and using of specific muteins that will satisfy the claimed requirement of tissue protection as broadly claimed. Additionally, since prevention of injury suggests stopping of the injury, and since EPO muteins reduce the injury or restore tissue function post retinal ischemic injury as exemplified in Example 18 of the instant specification, no guidance to a skilled artisan is provided for the prevention of injury from occurring.

20. Furthermore, although Applicants emphasize that the terms "restore" and "rejuvenate", are not related to new cellular growth, rather pertains to the tissue or organ function only, this explanation conflicts with the claim limitations of claim 57 that recites "restoring or rejuvenating **tissue** or tissue function" (emphasis

added). Applicant's argument is accepted to the extent of the rejuvenation or restoration of tissue function by S100E, R103E, K45D/S100E, or K45D, however, the claims are not enabled for the restoration or cells or tissues. As stated in the previous Office Action, and further based on the breadth of the amended claims, it is reiterated that EPO is capable of reducing inflammation-associated neuronal cell death, such as apoptosis or necrosis, but does not go so far as to implicate EPO as being able to induce new cellular growth, which would be necessary to restore or rejuvenate tissue. Undue experimentation would be required to rejuvenate a tissue using any of the mutein species as claimed.

21. Lastly, Applicant's reminder to the PTO about the distinction in jurisdiction of regulation followed by FDA and the PTO in terms of dosage and efficacy of the pharmaceutical composition is considered and agreed. However, the previous Office Actions make no mention of FDA approval, nor has the examiner indicated that the invention involves implausible scientific principles or that the pharmaceutical composition is unsafe for human consumption. The examiner understands that the "Patent and Trademark Office is not the FDA".

22. Specifically, proper analysis of the Wands factors was provided in the previous Office Action. Therefore, in view of the breadth of the claims still encompassing an enormous number of muteins, the lack of adequate guidance or evidence supporting a therapeutic effect of the same, the unpredictability in the art of biological effects of modifying EPO molecules by substitution of any amino acid, and the complex nature of the invention, one of skill in the art would

find that undue experimentation would be required to practice the claimed invention.

112-1st paragraph – Written Description

23. The rejections of claims 54-58, are applied to the amended claims, and new claims 71-73 for reasons of record in the Office Action dated 31 December 2007.

24. Applicant argues that the currently amended claims have defined regions that affect the erythropoietic activity of EPO, and mutations within this region yield EPO muteins that lack erythropoietic activity. Applicant further argues that specific mutein recombinant tissue protective cytokines are described in the instant specification and working examples demonstrating the reduced erythropoietic activity and the presence of tissue protective activity is exemplified in various examples. The instant specification also discloses a structure-function correlation of the muteins, so as to prove possession of the claimed invention at the time of filing. Thus Applicants assert that the rejection for lack of written description should be withdrawn.

25. Applicant's arguments have been fully considered but have not been found to be persuasive. The amended claims are limited to methods using mutein recombinant tissue protective cytokine molecules comprising the substitution of an amino acid in one or more positions of SEQ ID NOs: 1-4 of SEQ ID NO: 10, however, the claims still fail to recite a representative number of

EPO mutein species. Hence, the specification does not provide adequate written description of methods using an entire genus of EPO muteins capable of tissue protective activity along with reduced in vivo erythropoietic activity as broadly claimed. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. As stated in the previous Office Action, because the methods require the use of cytokine molecules that are defined only by broad functional limitations, the claims encompass a method of using a genus of cytokine molecules. Although, Applicant argues that muteins within the scope of the amended claims are provided on pages 32-35 and 47-49 of the instant specification, the muteins include mutations outside the claimed amino acid residues of 11-15, 44-51, 100-108 and 146-151 of the native EPO comprising SEQ ID NO: 10, that must be conserved for the EPO activity, as mutations in these regions can result in decreased erythropoietic activity. As stated in the previous Office Action, it is reiterated as follows:

> Accordingly, there is no means by which the artisan, given any of these cytokine molecules, would know whether it was a member of the genus that could be used in the claimed methods. The instant disclosure of the several specific mutein EPO species does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. Therefore, the claims are directed to subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed genus of molecules.

Therefore, only muteins S100E, R130E, R150E, R103E, K45D/S100E, K45D, and methods using the same, but not the full breadth of the claim meets the

written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

26. The rejection of claims 54-58 under 35 U.S.C. 102(e) as clearly anticipated by Brines et al. (International Publication No WO 02/053580 A2, filed on 28 December 2001, with a prior filing date for US Patent application number 09/753,132, of 29 December 2000) is applied to the amended claims and new claims 71-73, for reasons of record in the Office Action dated 31 December 2007.

27. The claims recite ex vivo method of protecting, maintaining or enhancing the viability of a responsive cell (neuronal or ganglion), or an organ comprising exposing said cell, tissue or organ to a pharmaceutical composition comprising a mutein tissue protective cytokine comprising the amino acid sequence of SEQ ID NO: 10, with a substitution of an amino acid residue at one or more position of SEQ ID NOs: 1, 2, 3 or 4, has reduced in vivo erythropoietic activity, and has

tissue protective activity (claims 54-56, 71). Claims 57-58 and 72-73 are drawn to an *in vivo* method of protecting against tissue injury, prevention of tissue injury, restoration or rejuvenation of tissue or tissue function, in a mammal using the above muteins, wherein the mammal has or is at risk of a large number of diseases and injuries, e.g. retinal ischemia.

28. Applicant argues that the International application publication '580 does not anticipate the claims as amended, because the reference generically discloses EPO muteins, however, does not teach the specific EPO muteins recited in the instant claims. Applicant further asserts that the reference does not disclose particular structural and functional features as claimed, i.e. mutations in 28 amino acids of the 165 amino acids of the mature EPO protein. Applicant, therefore, requests the withdrawal of the rejection.

29. Applicant's arguments are fully considered, but not found to be persuasive. Contrary to Applicant's allegation, Brines et al do teach the specific EPO muteins recited in the amended claims. The reference discloses EPO useful for the method can be altered in one or more amino acids within the four sequence lengths represented by SEQ ID NOs: 1-4 of the instant claims (see page 24). As Brines et al teach the structural and functional limitations of the amended claims, the reference anticipates the claimed invention.

Conclusion

30. No claims are allowed.

31. **THIS ACTION IS MADE FINAL**.

32. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

34. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

35. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through

Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
29 November 2008

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649